

Connecting via Winsock to STN

Welcome to STN International! Enter x:X

LOGINID:SSPTACMB1647

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JAN 12	Match STN Content and Features to Your Information Needs, Quickly and Conveniently
NEWS	3	JAN 25	Annual Reload of MEDLINE database
NEWS	4	FEB 16	STN Express Maintenance Release, Version 8.4.2, Is Now Available for Download
NEWS	5	FEB 16	Derwent World Patents Index (DWPI) Revises Indexing of Author Abstracts
NEWS	6	FEB 16	New FASTA Display Formats Added to USGENE and PCTGEN
NEWS	7	FEB 16	INPADOCDB and INPAFAMDB Enriched with New Content and Features
NEWS	8	FEB 16	INSPEC Adding Its Own IPC codes and Author's E-mail Addresses
NEWS	9	APR 02	CAS Registry Number Crossover Limits Increased to 500,000 in Key STN Databases
NEWS	10	APR 02	PATDPAFULL: Application and priority number formats enhanced
NEWS	11	APR 02	DWPI: New display format ALLSTR available
NEWS	12	APR 02	New Thesaurus Added to Derwent Databases for Smooth Sailing through U.S. Patent Codes
NEWS	13	APR 02	EMBASE Adds Unique Records from MEDLINE, Expanding Coverage back to 1948
NEWS	14	APR 07	CA/CAPLUS CLASS Display Streamlined with Removal of Pre-IPC 8 Data Fields
NEWS	15	APR 07	50,000 World Traditional Medicine (WTM) Patents Now Available in CAPLUS
NEWS	16	APR 07	MEDLINE Coverage Is Extended Back to 1947

NEWS EXPRESS FEBRUARY 15 10 CURRENT WINDOWS VERSION IS V8.4.2,  
AND CURRENT DISCOVER FILE IS DATED 15 JANUARY 2010.

NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS LOGIN Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN customer agreement. This agreement limits use to scientific research. Use for software development or design, implementation of commercial gateways, or use of CAS and STN data in the building of commercial products is prohibited and may result in loss of user privileges and other penalties.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 11:41:42 ON 27 MAY 2010

=> file medline biosis caplus embase  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.22	0.22

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 11:42:08 ON 27 MAY 2010

FILE 'BIOSIS' ENTERED AT 11:42:08 ON 27 MAY 2010  
Copyright (c) 2010 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 11:42:08 ON 27 MAY 2010  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 11:42:08 ON 27 MAY 2010  
Copyright (c) 2010 Elsevier B.V. All rights reserved.

=> s (GABA(w)A or gamma(w)amino(w)butyric(w)acid(w)A)  
L1 45722 (GABA(W) A OR GAMMA(W) AMINO(W) BUTYRIC(W) ACID(W) A)

=> s l1 and delta(w)subunit  
L2 717 L1 AND DELTA(W) SUBUNIT

=> s l2 and (express? or immunohistochem? or immunoblot?)  
L3 503 L2 AND (EXPRESS? OR IMMUNOHISTOCHEM? OR IMMUNOBLOT?)

=> s l3 and (A4B2D or alpha4beta2delta)  
L4 10 L3 AND (A4B2D OR ALPHA4BETA2DELTA)

=> dup rem l4  
PROCESSING COMPLETED FOR L4  
L5 7 DUP REM L4 (3 DUPLICATES REMOVED)

=> dis ibib abs l5 1-7

L5 ANSWER 1 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 2009048178 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18762200  
TITLE: Novel compounds selectively enhance delta  
subunit containing GABA A  
receptors and increase tonic currents in thalamus.  
AUTHOR: Wafford K A; van Niel M B; Ma Q P; Horridge E; Herd M B;  
Peden D R; Belelli D; Lambert J J  
CORPORATE SOURCE: Department of Molecular and Cellular Neuroscience, Merck  
Sharp & Dohme Research Laboratories, The Neuroscience  
Research Centre, Harlow, United Kingdom..  
waffordke@lilly.com  
CONTRACT NUMBER: C509923 (United Kingdom Biotechnology and Biological  
Sciences Research Council)  
SOURCE: Neuropharmacology, (2009 Jan) Vol. 56, No. 1, pp. 182-9.  
Electronic Publication: 2008-08-13.  
Journal code: 0236217. ISSN: 0028-3908. L-ISSN: 0028-3908.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200904  
ENTRY DATE: Entered STN: 6 Jan 2009  
Last Updated on STN: 3 Apr 2009  
Entered Medline: 2 Apr 2009

AB Inhibition in the brain is dominated by the neurotransmitter gamma-aminobutyric acid (GABA); operating through GABA(A) receptors. This form of neural inhibition was presumed to be mediated by synaptic receptors, however recent evidence has highlighted a previously unappreciated role for extrasynaptic GABA(A) receptors in controlling neuronal activity. Synaptic and extrasynaptic GABA(A) receptors exhibit distinct pharmacological and biophysical properties that differentially influence brain physiology and behavior. Here we used a fluorescence-based assay and cell lines expressing recombinant GABA(A) receptors to identify a novel series of benzamide compounds that selectively enhance, or activate alpha4beta3delta GABA(A) receptors (cf. alpha4beta3gamma2 and alpha1beta3gamma2). Utilising electrophysiological methods, we illustrate that one of these compounds, 4-chloro-N-[6,8-dibromo-2-(2-thienyl)imidazo[1,2-a]pyridine-3-yl benzamide (DS1) potentially (low nM) enhances GABA-evoked currents mediated by alpha4beta3delta receptors. At similar concentrations DS1 directly activates this receptor and is the most potent known agonist of alpha4beta3delta receptors. 4-chloro-N-[2-(2-thienyl)imidazo[1,2-a]pyridine-3-yl benzamide (DS2) selectively potentiated GABA responses mediated by alpha4beta3delta receptors, but was not an agonist. Recent studies have revealed a tonic form of inhibition in thalamus mediated by the alpha4beta2delta extrasynaptic GABA(A) receptors that may contribute to the regulation of thalamocortical rhythmic activity associated with sleep, wakefulness, vigilance and seizure disorders. In mouse thalamic relay cells DS2 enhanced the tonic current mediated by alpha4beta2delta receptors with no effect on their synaptic GABA(A) receptors. Similarly, in mouse cerebellar granule cells DS2 potentiated the tonic current mediated by alpha6betadelta receptors. DS2 is the first selective positive allosteric modulator of delta-GABA(A) receptors and such compounds potentially offer novel therapeutic opportunities as analgesics and in the treatment of sleep disorders. Furthermore, these drugs may be valuable in elucidating the physiological and pathophysiological roles played by these extrasynaptic GABA(A) receptors.

L5 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2008317535 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18480294  
TITLE: Ketamine, but not phencyclidine, selectively modulates cerebellar GABA(A) receptors containing alpha6 and delta subunits.  
AUTHOR: Hevers Wulf; Hadley Stephen H; Luddens Hartmut; Amin Jahanshah  
CORPORATE SOURCE: Carl-Ludwig Department of Physiology, University of Leipzig, D-04103 Leipzig, Germany.  
SOURCE: The Journal of neuroscience : the official journal of the Society for Neuroscience, (2008 May 14) Vol. 28, No. 20, pp. 5383-93.  
Journal code: 8102140. E-ISSN: 1529-2401. L-ISSN: 0270-6474.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200806

ENTRY DATE: Entered STN: 16 May 2008  
Last Updated on STN: 20 Jun 2008  
Entered Medline: 19 Jun 2008

AB Phencyclidine (PCP) and ketamine are dissociative anesthetics capable of inducing analgesia, psychomimetic behavior, and a catatonic state of unconsciousness. Despite broad similarities, there are notable differences between the clinical actions of ketamine and PCP. Ketamine has a lower incidence of adverse effects and generally produces greater CNS depression than PCP. Both noncompetitively inhibit NMDA receptors, yet there is little evidence that these drugs affect GABA(A) receptors, the primary target of most anesthetics. alpha6beta2/3delta receptors are subtypes of the GABA(A) receptor family and are abundantly expressed in granular neurons within the adult cerebellum. Here, using an oocyte expression system, we show that at anesthetically relevant concentrations, ketamine, but not PCP, modulates alpha6beta2delta and alpha6beta3delta receptors. Additionally, at higher concentrations, ketamine directly activates these GABA(A) receptors. Comparatively, dizocilpine (MK-801 [(+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d] cyclohepten-5,10-imine maleate]), a potent noncompetitive antagonist of NMDA receptors that is structurally unrelated to PCP, did not produce any effect on alpha6beta2delta receptors. Of the recombinant GABA(A) receptor subtypes examined (alpha1beta2, alpha1beta2gamma2, alpha1beta2delta, alpha4beta2gamma2, alpha4beta2delta, alpha6beta2gamma2, alpha6beta2delta, and alpha6beta3delta), the actions of ketamine were unique to alpha6beta2delta and alpha6beta3delta receptors. In dissociated granule neurons and cerebellar slice recordings, ketamine potentiated the GABAergic conductance arising from alpha6-containing GABA(A) receptors, whereas PCP showed no effect. Furthermore, ketamine potentiation was absent in cerebellar granule neurons from transgenic functionally null alpha6(-/-) and delta(-/-) mice. These findings suggest that the higher CNS depressant level achieved by ketamine may be the result of its selective actions on alpha6beta2/3delta receptors.

L5 ANSWER 3 OF 7 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2007429292 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 17395622  
TITLE: Rat alpha6beta2delta GABAA receptors exhibit two distinct and separable agonist affinities.  
AUTHOR: Hadley Stephen H; Amin Jahanshah  
CORPORATE SOURCE: Department of Molecular Pharmacology and Physiology, College of Medicine, University of South Florida, Tampa, FL 33612, USA.  
SOURCE: The Journal of physiology, (2007 Jun 15) Vol. 581, No. Pt 3, pp. 1001-18. Electronic Publication: 2007-03-29. Journal code: 0266262. ISSN: 0022-3751. L-ISSN: 0022-3751. Report No.: NLM-PMC2170852.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: (COMPARATIVE STUDY)  
Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200708  
ENTRY DATE: Entered STN: 27 Jul 2007  
Last Updated on STN: 10 Aug 2007  
Entered Medline: 9 Aug 2007

AB The onset of motor learning in rats coincides with exclusive expression of GABAA receptors containing alpha6 and delta subunits in the granule neurons of the cerebellum. This

development temporally correlates with the presence of a spontaneously active chloride current through alpha6-containing GABAA receptors, known as tonic inhibition. Here we report that the coexpression of alpha6, beta2, and delta subunits produced receptor-channels which possessed two distinct and separable states of agonist affinity, one exhibiting micromolar and the other nanomolar affinities for GABA. The high-affinity state was associated with a significant level of spontaneous channel activity. Increasing the level of expression or the ratio of beta2 to alpha6 and delta subunits increased the prevalence of the high-affinity state. Comparative studies of alpha6beta2delta, alpha1beta2delta, alpha6beta2gamma2, alpha1beta2gamma2 and alpha4beta2delta receptors under equivalent levels of expression demonstrated that the significant level of spontaneous channel activity is uniquely attributable to alpha6beta2delta receptors. The pharmacology of spontaneous channel activity arising from alpha6beta2delta receptor expression corresponded to that of tonic inhibition. For example, GABAA receptor antagonists, including furosemide, blocked the spontaneous current. Further, the neuroactive steroid 5alpha-THDOC and classical glycine receptor agonists beta-alanine and taurine directly activated alpha6beta2delta receptors with high potency. Specific mutation within the GABA-dependent activation domain (betaY157F) impaired both low- and high-affinity components of GABA agonist activity in alpha6betaY157Fdelta receptors, but did not attenuate the spontaneous current. In comparison, a mutation located between the second and third transmembrane segments of the delta subunit (deltaR287M) significantly diminished the nanomolar component and the spontaneous activity. The possibility that the high affinity state of the alpha6beta2delta receptor modulates the granule neuron activity as well as potential mechanisms affecting its expression are discussed.

L5 ANSWER 4 OF 7 MEDLINE on STN  
 ACCESSION NUMBER: 2007184474 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 17351635  
 TITLE: Reversal of neurosteroid effects at  
 alpha4beta2delta GABAA receptors triggers anxiety  
 at puberty.  
 AUTHOR: Shen Hui; Gong Qi Hua; Aoki Chiye; Yuan Maoli; Ruderman  
 Yevgeniy; Dattilo Michael; Williams Keith; Smith Sheryl S  
 CORPORATE SOURCE: Department of Physiology and Pharmacology, SUNY Downstate  
 Medical Center, 450 Clarkson Avenue, Brooklyn, New York  
 11203, USA.  
 CONTRACT NUMBER: P30 EY013079-079003 (United States NEI NIH HHS)  
 R01 EY008055-09 (United States NEI NIH HHS)  
 R01 EY013145-04 (United States NEI NIH HHS)  
 R01 NS041091-04 (United States NINDS NIH HHS)  
 SOURCE: Nature neuroscience, (2007 Apr) Vol. 10, No. 4, pp. 469-77.  
 Electronic Publication: 2007-03-11.  
 Journal code: 9809671. ISSN: 1097-6256. L-ISSN: 1097-6256.  
 Report No.: NLM-NIHMS18000; NLM-PMC1858651.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: (IN VITRO)  
 Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, N.I.H., EXTRAMURAL)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200706  
 ENTRY DATE: Entered STN: 28 Mar 2007  
 Last Updated on STN: 27 Jun 2007  
 Entered Medline: 26 Jun 2007  
 AB Puberty is characterized by mood swings and anxiety, which are often

produced by stress. Here we show that THP (allopregnanolone), a steroid that is released as a result of stress, increases anxiety in pubertal female mice, in contrast to its anxiety-reducing effect in adults. Anxiety is regulated by GABAergic inhibition in limbic circuits. Although this inhibition is increased by THP administration before puberty and in adults, during puberty THP reduces the tonic inhibition of pyramidal cells in hippocampal region CA1, leading to increased excitability. This paradoxical effect of THP results from inhibition of  $\alpha 4\beta 2\delta$  GABAA receptors. These receptors are normally expressed at very low levels, but at puberty, their expression is increased in hippocampal area CA1, where they generate outward currents. THP also decreases the outward current at recombinant  $\alpha 4\beta 2\delta$  receptors, and this effect depends on arginine 353 in the  $\alpha 4$  subunit, a putative site for modulation by  $\text{Cl}^-$ . Therefore, inhibition of  $\alpha 4\beta 2\delta$  GABAA receptors by THP provides a mechanism for the generation of anxiety at puberty.

L5 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 3  
 ACCESSION NUMBER: 2007374227 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 17521848  
 TITLE: GABAA receptors in the thalamus:  $\alpha 4$  subunit expression and alcohol sensitivity.  
 AUTHOR: Jia Fan; Pignataro Leonardo; Harrison Neil L  
 CORPORATE SOURCE: Department of Anesthesiology, Weill Medical College, Cornell University, New York, NY 10021, USA.  
 SOURCE: Alcohol (Fayetteville, N.Y.), (2007 May) Vol. 41, No. 3, pp. 177-85. Electronic Publication: 2007-05-23. Ref: 81  
 Journal code: 8502311. ISSN: 0741-8329. L-ISSN: 0741-8329.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200708  
 ENTRY DATE: Entered STN: 27 Jun 2007  
 Last Updated on STN: 16 Aug 2007  
 Entered Medline: 15 Aug 2007

AB The inhibitory neurotransmitter gamma-aminobutyric acid (GABA) has long been implicated in the anxiolytic, amnesic, and sedative behavioral effects of alcohol. A large number of studies have investigated the interactions of alcohol with GABA receptors. Many investigators have reported effects of "high concentrations" (50-100 mM) of alcohol on GABA-mediated synaptic inhibition, but effects of the "low concentrations" (1-30 mM) of alcohol normally associated with mild intoxication have been elusive until recently. A novel form of "tonic inhibition" has been described in the central nervous system (CNS) that is generated by the persistent activation of extrasynaptic gamma-aminobutyric acid type A receptors (GABAA-Rs). These receptors are specific GABAA-R subtypes and distinct from the synaptic subtypes. Tonic inhibition regulates the excitability of individual neurons and the activity and rhythmicity of neural networks. Interestingly, several reports show that tonic inhibition is sensitive to low concentrations of alcohol. The thalamus is a structure that is critically important in the control of sleep and wakefulness. GABAergic inhibition in the thalamus plays a crucial role in the generation of sleep waves. Among the various GABAA-R subunits, the  $\alpha 1$ ,  $\alpha 4$ ,  $\beta 2$ , and  $\delta$  subunits are heavily expressed in thalamic relay nuclei. Tonic inhibition has been demonstrated in thalamocortical relay neurons, where it is mediated by  $\alpha 4\beta 2\delta$  GABAA-Rs. These extrasynaptic receptors are highly sensitive to gaboxadol, a novel hypnotic, but insensitive to benzodiazepines. Tonic inhibition is absent in thalamic relay neurons

from alpha4 knockout mice, as are the sedative and analgesic effects of gaboxadol. The sedative effects of alcohol can promote sleep. However, alcohol also disrupts the normal sleep pattern and reduces sleep quality. As a result, sleep disturbance caused by alcohol can play a role in the progression of alcoholism. As an important regulator of sleep cycles, inhibition in the thalamus may therefore be involved in both the sedative effects of alcohol and the development of alcoholism. Investigating the effects of alcohol on both synaptic and extrasynaptic GABAA-Rs in the thalamus should help us to understand the mechanisms underlying the interaction between alcohol and sleep.

L5 ANSWER 6 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 2006067963 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 16452673  
TITLE: Delta subunit susceptibility variants  
E177A and R220H associated with complex epilepsy alter  
channel gating and surface expression of  
alpha4beta2delta GABAA receptors.  
AUTHOR: Feng Hua-Jun; Kang Jing-Qiong; Song Luyan; Dibbens Leanne;  
Mulley John; Macdonald Robert L  
CORPORATE SOURCE: Department of Neurology, Vanderbilt University Medical  
Center, Nashville, Tennessee 37212, USA.  
CONTRACT NUMBER: NS33300 (United States NINDS NIH HHS)  
SOURCE: The Journal of neuroscience : the official journal of the  
Society for Neuroscience, (2006 Feb 1) Vol. 26, No. 5, pp.  
1499-506.  
Journal code: 8102140. E-ISSN: 1529-2401. L-ISSN:  
0270-6474.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200604  
ENTRY DATE: Entered STN: 3 Feb 2006  
Last Updated on STN: 28 Apr 2006  
Entered Medline: 27 Apr 2006  
AB Most human idiopathic generalized epilepsies (IGEs) are polygenic, but  
virtually nothing is known of the molecular basis for any of the complex  
epilepsies. Recently, two GABAA receptor delta subunit  
variants (E177A, R220H) were proposed as susceptibility alleles for  
generalized epilepsy with febrile seizures plus and juvenile myoclonic  
epilepsy. In human embryonic kidney 293T cells, recombinant  
halphalbeta2delta(E177A) and halphalbeta2delta(R220H) receptor currents  
were reduced, but the basis for the current reduction was not determined.  
We examined the mechanistic basis for the current reduction produced by  
these variants using the halpha4beta2delta receptor, an isoform more  
physiologically relevant and linked to epileptogenesis, by characterizing  
the effects of these variants on receptor cell surface expression  
and single-channel gating properties. Expression of variant  
alpha4beta2delta(R220H) receptors resulted in a decrease in  
surface receptor proteins, and a smaller, but significant, reduction was  
observed for variant alpha4beta2delta(E177A) receptors. For  
both variants, no significant alterations of surface expression  
were observed for mixed population of wild-type and variant receptors.  
The mean open durations of alpha4beta2delta(E177A) and  
alpha4beta2delta(R220H) receptor single-channel currents were both  
significantly decreased compared to wild-type receptors. These data  
suggest that both delta(E177A) and delta(R220H) variants may result in  
disinhibition in IGEs by similar cellular and molecular mechanisms, and in

heterozygously affected individuals, a reduction in channel open duration of delta subunit-containing GABAA receptors may be the major contributor to the epilepsy phenotypes.

L5 ANSWER 7 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 2006571671 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 16844844  
TITLE: Effects of ethanol on tonic GABA currents in cerebellar granule cells and mammalian cells recombinantly expressing GABA(A) receptors.  
AUTHOR: Yamashita Megumi; Marszalec William; Yeh Jay Z; Narahashi Toshio  
CORPORATE SOURCE: Department of Molecular Pharmacology and Biological Chemistry, Northwestern University Medical School, 303 E. Chicago Ave., Chicago, IL 60611-3008, USA.  
CONTRACT NUMBER: R01 AA07836 (United States NIAAA NIH HHS)  
SOURCE: The Journal of pharmacology and experimental therapeutics, (2006 Oct) Vol. 319, No. 1, pp. 431-8. Electronic Publication: 2006-07-14.  
Journal code: 0376362. ISSN: 0022-3565. L-ISSN: 0022-3565.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200611  
ENTRY DATE: Entered STN: 27 Sep 2006  
Last Updated on STN: 3 Nov 2006  
Entered Medline: 2 Nov 2006  
AB The effects of ethanol on the GABA(A) receptors, which are regarded as one of the most important target sites of ethanol, are very controversial, ranging from potentiation to no effect. The delta subunit-containing GABA(A) receptors expressed in Xenopus oocytes were recently reported to be potently augmented by ethanol. We performed patch-clamp experiments using the cerebellar granule cells and mammalian cells expressing recombinant GABA(A) receptors. In granule cells, the sensitivity to GABA increased from 7 to 11 days in vitro. Furosemide, an antagonist of alpha6-containing GABA(A) receptors, inhibited GABA-induced currents more potently at 11 to 14 days than at 7 days. Ethanol at 30 mM had either no effect or an inhibitory effect on currents induced by low concentrations of GABA in granule cells. On alpha4beta2delta, alpha6beta2delta, or alpha6beta3deltaGABA(A) receptors expressed in Chinese hamster ovary cells, ethanol at 10, 30, and 100 mM had either no effect or an inhibitory effect on GABA currents. Ethanol inhibition of GABA(A) receptor was observed in all of the subunit combinations examined. In contrast, the perforated patch-clamp method to record the GABA currents revealed ethanol effects on the alpha6beta2delta subunits ranging from slight potentiation to slight inhibition. Ethanol seems to exert a dual action on the GABA(A) receptors and the potentiating action may depend on intracellular milieu. Thus, the differences between the GABA(A) receptors expressed in mammalian host cells and those in Xenopus oocytes in the response to ethanol might be due to changes in intracellular components under patch-clamp conditions.